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EXAMINER
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ART UNIT	PAPER NUMBER
1634	

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23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/560,761	PENNA ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-28 and 31-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 10/17/02, paper number 20. Claims 22, 23, 24, 27, 28, 31, 32, 33, 34, 35, and 36 have been amended and claims 1-21, 29, 30, 37, 38, and 39 have been cancelled. Claims 22-28 and 31-36 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not fully persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

2. Applicant's election of SEQ ID NO: 3 and SEQ ID NO: 4 with traverse in paper number 15, affirmed in paper number 20 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Oath/Declaration

3. The substitute Oath has been entered.

Priority

4. The first line of the specification was corrected by the examiner to recite that this application is a CIP of parent application 09/607460 (as indicated in the transmittal papers), and also to indicate that the parent application is abandoned. Priority for the instantly claimed

invention is not granted to the parent application because the parent application does not provide adequate support under 112 1st paragraph.

Information Disclosure Statement

5. The a number of citations listed on the information disclosure statements filed 6/14/00, 6/23/00, and 11/6/00 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citations of references that are identified by title and "accession numbers" are not complete. These citations do not provide the name of the database whose accession numbers are represented. The content of all references that are properly cited have been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22-28 and 31-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-28 and 31-36 are rejected over the recitation of "phytyl/prenyltransferase protein" and "phytyl/prenyltransferase polynucleotide." The specification does not provide a

clear definition which identifies these proteins, and thus it is not possible to determine the metes and bounds of these claims. It is unclear from the specification what is required of a protein or polynucleotide in order for it to be characterized as a "phytyl/prenyltransferase" protein or polynucleotide. It is not clear if the encoded polypeptide must demonstrate transferase activity at all in order to be considered a "phytyl/prenyltransferase," or if this phrase encompasses any polynucleotides that would hybridize to or have homology to a protein referred to in the claims as "phytyl/prenyltransferase" polynucleotide (such as SEQ ID NO: 3), even if they lacked function as a transferase. Even if an activity is required, it is unclear from this nomenclature if applicant intends that the polynucleotide encode a polypeptide that has both phytyltransferase and prenyltransferase activity or if only one of these activities is sufficient. The specification never clearly defines this term, and appears to use "phytyl/prenyltransferase" interchangeably with prenyltransferase alone (see page 40 where a heading indicates "Confirmation of prenyltransferase nature" and then discusses a phytyl/prenyltransferase assay to accomplish this goal). It is therefore not clear what polynucleotides are included within the metes and bounds of these claims.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 22, 24, 25, 26, 27, 31, 33, 34, and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22, 24, 25, and 26, generically recite methods for modulating the level of phytyl/prenyltransferase protein in a plant wherein the methods utilize a phytyl/prenyltransferase polynucleotide. Claim 27 recites a method for modulating the level of tocopherol in a plant which utilize a phytyl/prenyltransferase polynucleotide. These claims do not recite any structural characteristics of the recited phytyl/prenyltransferase proteins and polynucleotides. Claims 31, 33, 34, and 36 are directed to methods for modulating the level of a phytyl/prenyltransferase protein in a plant which comprise transforming a plant cell with a phytyl/prenyltransferase polynucleotide and growing the plant cell under conditions to produce a regenerated plant, wherein the phytyl/prenyltransferase is selected from polynucleotides having at lease 70% sequence identity to SEQ ID NO: 3 and polynucleotides which selectively hybridize to SEQ ID NO: 3.

However, with regard to SEQ ID NO: 3 (the elected invention), the instant specification only describes a single polynucleotide, that is SEQ ID NO: 3. The specification has also demonstrated that instant SEQ ID NO: 9 has the ability to modulate tocopherol synthesis in Synechocystis.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a phytyl/prenyltransferase polynucleotide sequence having SEQ ID NO: 3 and a phytyl/prenyltransferase polynucleotide sequence having SEQ ID NO: 9. The

subject matter which is claimed is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed methods which utilize phytyl/prenylthransferase polynucleotides. With regard to the elected invention, the specification provides only two proteins and a two cDNA's encoding these protein and does not specifically teach or describe any other polynucleotides that are related to SEQ ID NO: 3 within the limitations of the rejected claims. The specification provides no guidance as to how or where the disclosed polynucleotide can be modified yet still maintain the functionality required for the instant methods. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the instant specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved

> until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

For the instantly elected claims, only SEQ ID NO: 3 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate written description of phyty/prenyltransferase polynucleotide which has nucleotides modified by addition, insertion, deletion, substitution or inversion with respect to SEQ ID NO: 3 or SEQ ID NO: 9 but retaining correlative function in the claimed methods.

10. Claims 22-28 and 31-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (A) methods for increasing the level of polypeptides encoded by instant SEQ ID NO: 3 or instant SEQ ID NO: 9 in a plant, (B) methods for increasing the level of and tocopherols in a plant wherein either (A) or (B) include a step of transforming the plant with instant SEQ ID NO: 3 or SEQ ID NO: 9 in the sense orientation, does not reasonably provide enablement for methods which utilize other polynucleotides or methods which utilize SEQ ID NO: 3 or SEQ ID NO: 9 in the anti-sense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that with regard to specific sequences, a restriction requirement was set forth, and applicant elected methods which utilize SEQ ID NO: 3.

These claims are drawn to methods for modulating the level of a phytyl/prenyltransferase protein in a plant and methods for modulating the level of tocopherol in a plant, both of these methods comprising stably transforming a plant cell with a phytyl/prenyltransferase polynucleotide operably linked to a promoter and growing the plant cell to regenerate a plant which has the appropriate component modified. Claims 23, 28, 30, and 31-36 each recite polynucleotide sequences for use in this method, some reciting specific sequences and some broadening the recitation to include polynucleotides which hybridize to or have homology to the specifically disclosed sequences. All of the claims encompass methods wherein the transgene is introduced in either the sense or antisense orientation.

The working examples in the specification demonstrate the ability of two different polynucleotides to effect tocopherol production. The first one, instant SEQ ID NO: 9 is a so-called phytyl/prenyltransferase that was isolated from Synechocystis (referred to in the specification as SLR1736). The specification demonstrates that the polypeptide encoded by SEQ ID NO: 9 possesses activity which results in the modulation of the level of tocopherols in cells. Specifically, when Synechocystis mutants with a disrupted SLR1736 gene were assayed, no tocopherol synthesis was observed, as opposed to wild type Synechocystis which produce tocopherol (p. 33). Applicant specifically teaches that the disruption of this gene did not demonstrate any effect on the activity of plastoquinones, suggesting that there is more than one prenyltransferase active in these cells (p. 33). Applicant teaches the isolation of genes from other plants which have sequence similarity to the SLR1786 gene (including SEQ ID NO: 3), but applicant does not teach that SLR1736 nor any of the other genes definitively encode a phytyl/prenyltransferase, wherein such a designation denotes any particular activity other than to

function in the pathway for the production of tocopherols. The specification does not provide any polynucleotides that have a demonstrated ability to modulate plastoquinones.

Applicant teaches soybean plants transformed with SEQ ID NO: 3 (i.e. the polynucleotide encoding SEQ ID NO: 4) in the positive (sense) orientation (see examples pages 55-71). Applicant provides the tocopherol/oil ration in somatic embryos produced from 33 different transformation events (pages 60-61). Applicant suggests that the normal range for such ratios would be from 2-5, and that the ratio would be higher than 5 if over-expression of the phytyl/prenyltransferase has increased the tocopherol production in the plants. Of the 33 ratios provided in Table 5, about a third of them were found to have tocopherol/oil ratios above the normal range. Applicant has thus demonstrated a method of increasing tocopherol levels in transgenic plants by transforming them with instant SEQ ID NO: 3, considering the ability of one to screen the transformed plant lines for the desired phenotype.

The specification has not provided any examples of methods for reducing the level of phytyl/prenyltransferase protein in a plant or methods for modulating the level of tocopherol in a plant that utilize transformation of plant cells with antisense constructs.

It is noted that the prior art provides methods which comprise transforming plant cells with nucleic acids encoding geranylgeranyl pyrophosphate (GGPP) synthase which is a phytyl/prenyltransferase protein (Ausich *et al.*). GGPP synthase is a known prenyltransferase protein (see the disclosures of Hefner et al. (1998), Ericsson et al. (1998) and Jiang et al (1993) which specifically teach that GGPP synthase is a prenyltransferase). These plants are also considered to be within the scope of the claimed invention by virtue of their presence in the prior art.

The state of the art for the isolation of cDNA or genomic clones with a defined functionality is highly unpredictable. In this case, the isolation of cDNA or genomic clones that are phytyl/prenyltransferase nucleic acids is complicated by the fact that there is not a clear definition in the claims of what the terminology encompasses. Applicant has isolated and characterized two polynucleotides that are clearly involved in tocopherol synthesis, namely SEQ ID NO: 3 and SEQ ID NO: 9. Applicant has not demonstrated that the ability to modulate tocopherol synthesis in transgenic plants is a property of all genes encoding phytyltransferases or prenyltransferasesgenes. It is not clear from the specification how the other isolated genes are structurally related to SEQ ID NO: 3 or SEQ ID NO: 9. Thus, it is not clear that methods utilizing these genes would accomplish the goals set out in the preamble of these claims.

Moreover, it is noted that the instant claims encompass methods which utilize nucleic acids that are related to SEQ ID NO: 3 based on hybridization or homology. However, Applicant provides no guidance for the regions of the disclosed SEQ ID NO: 3 which are essential or sufficient to modify tocopherol production in transgenic plants, or which are essential or sufficient to encode a phytyl/prenyltransferase. In the absence of such guidance, undue trial and error experimentation would be required to screen the vast number of different polynucleotides with 70% homology to or that would hybridize to SEQ ID NO: 3 to identify those which encode an active phytyl/prenyltransferase, especially in light of the fact that it is not clear from the specification that SEQ ID NO: 3 is a phytyl/prenyltransferase or how to identify such a molecule.

Furthermore, it is noted that many of the generic claims recited herein encompass the modulation of all phytyl/prenyltransferases in all plants. Within such a genus, there are hundreds

of thousands of possible phytyl/prenyltransferases, considering that such proteins would be present in all plants, and that there would likely be more than one enzyme in each species of plant with such activity. Applicant's own disclosure teaches that there are likely multiple prenyltransferases in the cyanobacteria Synechocystis, and further teaches page 41 that it is important to determine if one or two prenyltransferases are present in higher plants for tocopherol and plastoquinone biosynthesis. Since the two examples were did not demonstrate any modulation of plastoquinone levels, and the specification teaches that the phytyl/prenyltransferases are also active in the production of plastoquinones, this suggests that there are other undiscovered phytyl/prenyltransferases in Synechocystis and maize, as well as those undisclosed and undiscovered in other plants.

The state of the art for modification of gene expression or of phenotypic characteristics in plants by genetic transformation is highly unpredictable and hence significant guidance is required to practice the art without undue experimentation. It is clear from the specification that applicant is able to increase the level of instant SEQ ID NO: 3 or SEQ ID NO: 9 in transgenic plants, and that such an increase results in an increase in tocopherol production. However, the modulation of enzyme activity and achievement of a particular phenotype by antisense constructs is much less predictable. Indeed, the knowledge in the prior art would enable the skilled artisan to make transgenic plants with antisense constructs of SEQ ID NO: 3 or SEQ ID NO: 9, but it is highly unpredictable what effect these constructs would have on the transformed plant. The response of a transgenic plant to an antisense construct is dependent upon a number of factors, one is the sequence specific hybridization of the antisense transcript to some expressed nucleic acid in the transformed plant. For example, Elomaa et al. (1996, enclosed herewith) teach that

the degree of inhibition by an antisense transgene was dependent on homology between the antisense and the target genes. However, in the instant case, applicant has not provided any guidance as to what plants would contain sequences that are sufficiently homologous to instant SEQ ID NO: 3 or instant SEQ ID NO: 9 such that either of these would be successful at inhibiting the production of any target protein, let alone a target protein that would decrease the production of a phytyl/prenyltransferase protein or tocopherol. Furthermore, it is difficult to predict that an antisense construct will even decrease the production of any target of interest. For example, Colliver et al. teach an increase in transcripts following antisense transformation (1997, Plant Molecular Biology 35: 509-522, page 519, left column, second paragraph). Finally, even if inhibition of a transcript of interest was observed, it is highly unpredictable whether or not that inhibition will have the desired effect on the phenotype. For example, Majeau et al. teach that although antisense expression of a transgene resulted in 99% of carbonic anhydrase activity inhibition, this did not effect the CO2 assimilation, as would have been expected (Plant Molecular Biology, 1994, 25(3):377-85). In the instant case, applicant has even suggested that plants may contain more than one enzyme that has similar function to those encoded by instant SEQ ID NO: 3 or SEQ ID NO: 9. It is unpredictable whether these other enzymes may mask the effect of the antisense construct for example. In genetically modified plants, the introduced transgenes are sometimes not expressed, and they can also result in co-suppression effects. None of these effects are predictable, and the mechanisms of gene silencing are still not fully understood. Moreover, the phenotypic characteristics that will result from expression of a given DNA construct cannot be reliably predicted. In fact, often the expected phenotypic result is not

achieved. For example, the instant specification teaches that the blocking of the SLR1736 gene had no effect on plastoquinones when such effects would have been expected.

Given the unpredictability in the art of plant transformation to obtain a specified phenotype, the instant invention is not enabled given the lack of guidance in the specification with regard to what nucleic acids other than SEQ ID NO: 3 or SEQ ID NO: 9 can be expected to result in a modulation of phytyl/prenyltransferase levels or tocopherol levels. In the absence of such guidance, undue trial and error experimentation would be required to screen through the myriad of different DNA constructs and the vast number of transgenic plants to determine how to carry out the methods of the claimed invention. When all of the above is weighed, it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims.

It is note that each of the claims recites phytyl/prenyltransferase proteins and nucleic acids. However, it is unclear from the specification precisely what the limiting characteristics of such a protein are. The instant specification has demonstrated that SEQ ID NO: 3 and SEQ ID NO: 9 play a role in tocopherol regulation in plants, but they have not demonstrated that either of these is a phytyl/prenyltransferase, per se, thus, even if claim 28, for example, were limited to recite that SEQ ID NO: 3 is in the sense orientation, it would still be problematic in light of the recitation that SEQ ID NO: 3 is a phytyl/prenyltransferase polynucleotide, since no particular activity has been demonstrated for this polynucleotide

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 22, 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ausich *et al.* (US 5684238).

Ausich *et al.* teach a method for modulating the level of geranylgeranyl pyrophosphate (GGPP) synthase (which is a phytyl/prenyltransferase protein) in a plant comprising stably transforming a plant cell with a polynucleotide encoding GGPP operably linked to a promoter in the sense orientation and growing the plant cell under conditions to produce a regenerated plant capable of expressing the polynucleotide for a time sufficient to modulate the level of phytyl/prenyltransferase protein in the plant (Example 3, Col. 44-46). Ausich *et al.* teach that the plants produced by this method showed the presence of GGPP synthase, thus the GGPP synthase protein was increased in the plant (Col. 46, lines 35-40). Furthermore, Ausich *et al.* teach that these methods can be used to transform alfalfa (Col. 6, line 2).

Response to Remarks

With regard to the previously submitted Information Disclosure Statements, Applicant argued in the response that there is no requirement listed in the rules or the MPEP to list the database whose accession numbers are listed in the information disclosure statements, requesting that the examiner cite the precise language that requires applicant to accept the burden and expense of resubmitting the disclosure statements to include the database name. Rule 1.98(b)(5) requires that publications be identified by publisher, author, title, pages and place of publication. The rule does not specifically address records from a database, but this requirement is

understood to include the publisher of the database, which applicant's disclosure statements do not list. The recitation of simply the accession number is not useful for identifying a record in a database unless it is known from what database the record has been retrieved. Otherwise, the accession number is arbitrary. Contrary to Applicant's assertion, the accession number, even with the name of the submitter, year and source species, is not sufficient to retrieve the record without knowledge of within which database the record is housed. This is analogous to listing a page number for a reference without telling what book or journal contains the cited page.

The rejections have been modified to address some additional concerns identified by the examiner. Thus, this action is non-final.

Applicant's remarks are addressed insofar as they apply to the new rejections.

Applicant argues that the phrase "phytyl/prenyltransferase polynucleotide" or "phytyl/prenyltransferase polypeptide" would be clear based on the recitation on page 4 of the specification that recites "The present polypeptides catalyze the condensation of homogentistic acid with phytyldiphosphate or geranylgeranyl pryophosphate to produce the first intermediates in tocopherol or tocotrienol synthesis, respectively." However, this argument is not persuasive, because it is not defining the phrase "phytyl/prenyltransferase." Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The rejection is maintained and further clarified herein.

All other 112 2nd paragraph rejections are withdrawn in light of applicant's amendments and arguments.

With regard to the written description rejection, applicant argues that it is well within the ability of one of skill in the art to produce polynucleotide sequences within the limitations of the claims. Thus, applicants suggest that with regard to written description they merely need to communicate to those skilled in the art that the claimed subject matter is intended to be part of their invention. The examiner disagrees. The court has made it clear that with regard to chemical compounds, the standard for written description is possession, not enablement or intent to claim. "While we have no doubt a person so motivated would be enabled by the specification to make it, this is beside the point for the question is not whether he would be so enabled but whether the specification discloses the compound to him, specifically, as something appellants actually invented. We think it does not." In Re Ruschig, 379 F.2d 990, 995, 154 U.S.P.Q. 118, 123 (CCPA 1967). Furthermore, the court stated "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The Regents of the University of California v. Eli Lilly & Co., 43 U.S.P.Q.2d 1406 (Federal Circuit 1997). In the instant case, although applicant have provided a general descriptor of the polynucleotides to be used in the instant invention and a beginning structure (i.e. a recited relationship to instant SEQ ID NO: 3) these even taken together are not sufficient to convey possession of the entire possible group of all of the nucleic acids that have 70% identity to or would hybridize to instant SEQ ID NO: 3 that are encompassed by the instant claims. The specification has not demonstrated a correlation between having homology to SEQ ID NO: 3 or hybridizing to SEQ ID NO: 3 and any particular activity. There is no such known correlation discussed in the specification nor disclosed that would lead the skilled artisan to be able to envision all of the members of the genus of nucleic acids that have 70% identity to or

hybridize with instant SEQ ID NO: 3 and are also phytyl/prenyltransferase nucleic acids encoding phytyl/prenyltransferase proteins.

The recitation that the polynucleotides used in the instant invention are phytyl/prenyltransferase polynucleotides is not a recitation of a function such that a structure function relationship is set forth in the claims, because no function is set forth in the claims, merely that the nucleic acids must be this type. It is not clear in the claims if this type must possess a particular activity, and if so, what that activity is, as is discussed previously in the 112 2nd paragraph rejection. Again applicant's reference to the specification at page 4 which recites a very specific activity for the "polypeptides of the present invention" is non-limiting to the claims.

Applicants argue that physical and chemical properties associated with the sequences utilized in the methods are defined by hybridization conditions to the disclosed sequence beginning on page 12, line 30 of the specification and structural variants are described in the specification at page 9, lines 7-21 such that the skilled artisan could readily visualize that the applicant was in possession of the invention claimed. The section of the specification cited at page 12 discussed typical hybridization conditions, and that at page 9 discusses very broadly discusses different types of variants that are possible. This is not a demonstration of possession of the invention, but instead a description of conditions for an assay and what may exist. The applicant has provided no description of structural features that are common to all phytyl/prenyl transferases that hybridize to or have homology with instant SEQ ID NO: 3.

Applicant argues that the examiner has misapplied Fiers v. Sugano in support of the rejection because the instant specification provides a complete DNA sequence and methods for

isolating the sequence, citing the specification at page 42. The examiner agrees that the complete SEQ ID NO: 3 is described. Applicant has not described the variants and homologues of SEQ ID NO: 3 that are claimed and are at issue. With regard to these sequences, the Fiers decision is certainly relevant because it addresses precisely the issue of claiming sequences that Applicant has not demonstrated that Applicant possesses.

Applicant's arguments with regard to the ability of SEQ ID NO: 3 to increase the level of tocopherol in a transgenic plant are persuasive, and the scope of enablement rejection has been modified to indicate as much.

Applicant argues that the specification teaches sequences with demonstrated phytyl/prenyltransferase function and cites art that teaches prenyltransferases from seven organisms, and that consequently one of skill in the art would be well apprised of how to make and use the presently claimed invention. However, applicant's arguments do not address each of the factors set forth in the enablement rejection. The mere fact that some nucleic acid sequences encoding prenyltransferases were known does not provide enablement for methods for modulating the levels of all phytyl/prenyltransferases in all plants, as discussed in the enablement rejection.

Applicant argues that it is believed that the phytyl/prenyltransferase function of SEQ ID NO: 3 is fully supported by it's homology to known phytyl/prenyltransferase polynucleotides, the presence of conserved regions, and its demonstrated ability to increase tocopherol levels in transformed plant tissue. While the specification does in fact demonstrate the third feature cited, the first two are not provided in the specification and cannot be properly evaluated by the examiner.

Applicant cites Lopez et al. as teaching that GGPP synthase is an enzyme which can react with phytyl/prenyltransferase, not a homolog to phytyl/prenyltransferase. However, Lopez et al. do not discuss GGPP synthase, but instead the section cited by applicant is discussing that the polyprenoltransferase bchG is catalyzing a process wherein an ester is being formed between bacteriochlorophyllide a and GGPP itself. Lopez et al. do not discuss GGPP synthase. Contrary to applicant's argument, a number of prior art references describe the activity by which GGPP synthase functions as prenyltransferase activity (see, for example, Hefner et al. (1998), Ericsson et al. (1998) and Jiang et al (1993)) . For example, Ericsson et al. state that "The prenyltransferases catalyze three different types of reactions. One type, typified by farnesyl diphosphate (FPP) synthase and geranylgeranyl diphosphate (GGPP) synthase, catalyze the sequential condensation of isopentenyl diphosphate with allylic diphosphate to synthesize linear prenyl diphsophates…(p. 1731)." Thus, the examiner concludes that insofar as "phytyl/prenyltransferases nucleic acids" includes all nucleic acids that encode prenyltransferase enzymes, the teachings of Ausich et al. are considered to be within the scope of the instantly claimed invention.

Applicants arguments regarding the teachings of the prior art and the specification (page 21) leading to the conclusion that "a rational scheme for identifying sequences encompassed by the claims 31, 33, 34, and 36 has been provided in the specification" is not persuasive for reasons previously discussed. First, it is unclear what nucleic acids are even encompassed by the claims (as in the issues discussed in the 112 2nd rejection), and thus the identification of such nucleic acids for use in the claimed invention is highly unpredictable. Second, each of the claims encompass the modulation of phytyl/prenyltransferases in any plant via use of any sense or

antisense constructs. Given the large number of possible polynucleotides that fall within the recitation of claims 31, 33, 34,and 36, it would be difficult to predict how these would function in plants, in either sense or antisense constructs, since the proteins encoded by the homologues of instant SEQ ID NO: 3 may or may not have activity of a phytyl/prenyltransferase.

Applicant reminds the examiner that the Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is undue, citing In re Wands. The examiner is well aware of the court's guidance, and considered each of the following factors in formulating the rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary. The relevant factors are discussed in the rejection.

Applicant argues that the quantity of experimentation amounts to two steps to identify sequences at issue, that is to generate the nucleic acid sequences and to assay for modulated activity. However, applicant does not address the fact that within the scope of the polynucleotides recited in the claimed methods, there are hundreds of thousands of possible variants and there is no guidance provided in the specification as to which ones of these might or might not be able to modulate any enzyme activity in transgenic plants, either by causing an increase or decrease in enzyme activity. While some experimentation in screening for polynucleotides may be routine, in this case there is a lack of guidance that would overcome the unpredictability of the matter, and the experimentation is undue, for all of the reasons discussed in the rejection.

The rejection under 112 1st paragraph for scope of enablement is therefore maintained.

With regard to the 102 rejections over Ausich et al., Applicant argues that GGPP sythase is not a phytyl/prenyltransfase, stating, "Quite simple, a synthase does not function as a transferse." However, contrary to applicant's argument, a number of prior art references describe the activity by which GGPP synthase functions as prenyltransferase activity (see, for example, Hefner et al. (1998), Ericsson et al. (1998) and Jiang et al (1993)) . For example, Ericsson et al. state that "The prenyltransferases catalyze three different types of reactions. One type, typified by farnesyl diphosphate (FPP) synthase and geranylgeranyl diphosphate (GGPP) synthase, catalyze the sequential condensation of isopentenyl diphosphate with allylic diphosphate to synthesize linear prenyl diphsophates…(p. 1731)." Thus, the examiner concludes that insofar as "phytyl/prenyltransferases nucleic acids" includes all nucleic acids that encode prenyltransferase enzymes, the teachings of Ausich et al. are considered to be within the scope of the instantly claimed invention, as discussed in the 102(b) rejection.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

January 8, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Einsmann
Examiner
Art Unit 1655